Human Trials Begin for Malaria Vaccine

Although still in the early stages, testing of vaccines builds hopes for immunization

THE quest for an effective vaccine against malaria has progressed to the stage of human trials. Researchers at the University of Maryland School of Medicine have begun a sequence of trials with human volunteers that could lead within 2 years to clinical field trials of a prototype vaccine in developing countries where malaria is on the rise. First-phase tests with human volunteers conducted at Maryland have established the safety of a candidate vaccine against one type of malaria.

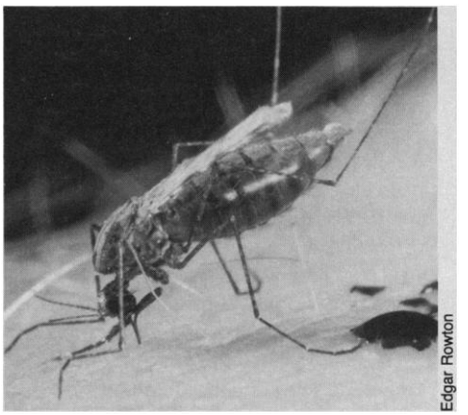
Myron Levine, the physician supervising the trials at the vaccine development center at Maryland, says that a decision to proceed to a second-phase trial aimed at showing the vaccine's effectiveness in preventing infection with the disease depends on whether current analyses indicate that the vaccine has created a sufficiently strong immune response in test subjects. If the findings are favorable, a form of the malaria parasite will be introduced into the bloodstream of vaccinated volunteers to determine whether the vaccine is effective in neutralizing invasion to the liver and forestalling development of the disease.

The program is sponsored by the U.S. Agency for International Development, which has been a major backer of malaria vaccine development since the middle 1960s. The need for a vaccine is urgent because of the return of the disease as a major health threat in many developing countries. Mounting resistance of the mosquito vector of the disease to pesticides and of the malaria parasite to antimalarial drugs has caused the resurgence. AID estimates that 150 million cases of malaria occur annually.

While research on malaria vaccines is going forward in a number of countries, the only other instance of full-scale first-phase testing in humans apparently is in an Army-sponsored program based at Walter Reed Army Institute of Research in Washington, D.C. A test of a prototype vaccine in 15 volunteers was initiated in March 1986. The vaccine proved to be safe and produced an antibody response in the volunteers. In all but one case, however, the response was not as strong as seen in inhabitants of hyperendemic areas who have acquired immunity to malaria through direct exposure to the disease.

Jeffrey Chulay, chief of the department of immunology at Walter Reed, says that a request for an amendment to the protocol is being considered that would permit injection of the volunteers with a further booster shot of the vaccine. If the response is as strong as expected, the volunteers would be subjected to a malaria "challenge."

The vaccine now under test at Maryland is aimed at *Plasmodium falciparum*, which causes the deadliest of human malarias. Falciparum malaria is regarded as particularly dangerous because in some areas of Asia, Africa, and Latin America it has become resistant to chloroquine, the most widely available and cheapest of antimalarial drugs, and no adequate substitute is available.

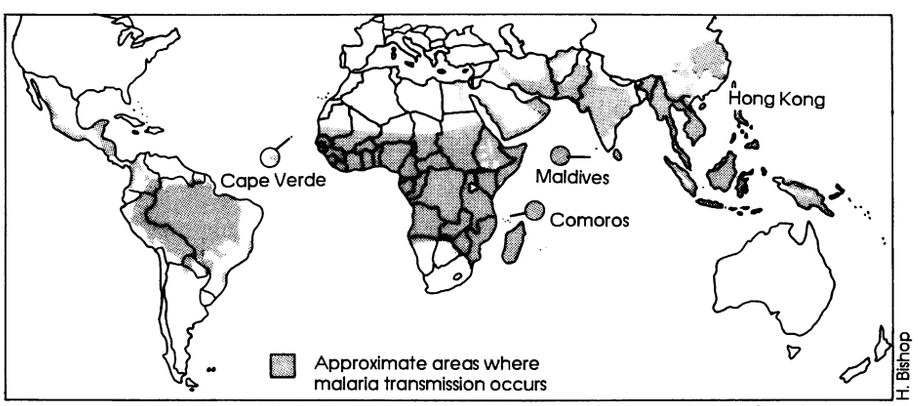


Point of contact. *Malaria is transmitted when parasites enter bloodstream as female* Anopheles *mosquito (above) bites human. Cycle is completed when infected human is bitten by mosquito.*

Success with the two-stage trials at Maryland would lay the groundwork for third-phase clinical field trials in areas where malaria is endemic. AID hopes to arrange clinical field trials of a vaccine in Asia, Africa, and Latin America. The agency is looking initially for two sites in Asia. AID teams will travel in April to Thailand and Papua New Guinea for talks with governments there on arrangements for trials. Some 18 months to 2 years of epidemiological work is regarded as essential in preparation for the trials.

The vaccines being tested at both Maryland and Walter Reed are active against the parasite's sporozoite form, the form it maintains between the time it enters the human bloodstream from the bite of an infected mosquito and the time it penetrates the liver. In the liver, the parasite changes into thousands of so-called merozoites that erupt from the liver into the bloodstream and enter red blood cells where they continue to multiply. The vaccine in the Walter Reed program is based on an antigen derived by recombinant DNA techniques. The vaccine being tested at Maryland is based on a synthetic peptide.

Only in the past decade have researchers using the techniques of biotechnology made solid progress toward development of a malaria vaccine (*Science*, 9 November 1984, p. 679). Such a vaccine would be the first for a parasitic disease as distinct from diseases caused by bacteria or viruses. Research leading to the identification of the principal antigens that trigger release of antibodies against sporozoites has permitted the most rapid progress toward vaccine development. Trials on vaccines directed at merozoites are also being planned.



Adapted from World Health Organization map

Malaria projection. *Shaded areas on map show areas where malaria is transmitted, according to World Health Organization.*

The antisporozoite vaccine used in the Maryland trials was produced by Hoffmann–La Roche based on work done by a research team headed by Ruth and Victor Nussenzweig at New York University Medical Center. Prospects for manufacture of the vaccine were clouded for a period (*Science*, 4 February 1983, p. 467). The World Health Organization objected, expressing misgivings about patent rights, when Genentech, a biotechnology firm in South San Francisco, expressed interest in gaining an exclusive license to produce the vaccine. Hoffmann–La Roche subsequently obtained a license as prospective manufacturer of the vaccine and AID sources say that an agreement was made providing for preferential pricing of the vaccine for both AID and WHO that both organizations find satisfactory.

If field trials of a vaccine aimed at falciparum sporozoites are successful, a further trial phase aimed at developing the vaccine as a public health tool would be necessary. Such matters as dosages and frequency of shots would have to be established. It is expected that commercial companies would then be interested in producing a falciparum sporozoite vaccine. Such a vaccine would protect tourists and military personnel against infection with that type of malaria. A merozoite vaccine, however, would be required to protect people already infected with malaria from recurrences of the disease.

James Erickson, project manager for AID's malaria program, says that a vaccine active against sporozoites would be an important advance, but would represent only a first step toward developing what AID envisions as a satisfactory vaccine. The goal, says Erickson, is a polyvalent vaccine, a "cocktail" effective against different forms of the parasite and all types of malaria—malaria in humans is of four main types. Developing a fully effective, polyvalent vaccine is likely to take a decade, says Erickson. ■

JOHN WALSH

Chip Makers Plan Research Center

Leaders of the U.S. semiconductor industry announced on 5 March that they will invest jointly in a major new center to improve their manufacturing skills and make their products more competitive.

They have not fixed the cost of the project, to be known as "Sematech," an acronym for Semiconductor Manufacturing Technology Institute. If it adheres to the recommendations made by a recent Defense Department inquiry (*Science*, 15 August 1986, p. 712), the cost will be over $1 billion, perhaps $2 billion. Although all member companies will contribute, a spokesman for the Semiconductor Industry Association said, a major share will have to come from the federal government.

Charles E. Sporck, president of the National Semiconductor Corporation, formally unveiled the plan in Washington last week. His announcement came after a long and intense debate within the industry over what should be done to make U.S. companies more competitive. It is a sign of independence, Sporck said, that the companies have not come to Washington seeking help until now.

The internal debate focused on what should be put in the new facility. Some smaller companies wanted to install a high-volume production line at Sematech and get International Business Machines to promise to use its output. IBM reportedly declined, although it did agree to contribute a large share toward the new venture. Others wanted to focus on methods for rapidly introducing new designs into production, leaving the manufacturing to be done by individual companies. This view seems to have the upper hand.

Sporck said it will take until June to work out an operating plan. By then, Sematech should have a director, a site, an agenda, clearance from the antitrust division of the Justice Department, and a funding goal. None of these exist now. It is clear, however, that Sematech will focus on production equipment and large-scale manufacturing techniques to make commercial, not military, products.

This move is the latest in a series of steps taken by U.S. silicon chip companies to strengthen their position in the world market, which is eroding rapidly. According to Charles Ferguson of MIT's Center for Technology, Policy, and Industrial Development, the U.S. companies are headed on a decline that will not be reversed easily. He said in testimony to a Senate subcommittee on 26 February that Japanese efforts on x-ray lithography, "which will probably dominate semiconductor production by the mid-1990s, dwarf those of the United States." Japanese companies are already on a par with or ahead of U.S. companies in gallium arsenide research, laser systems, and optoelectronics. Unless there is a drastic change in the rate of investment in research and development in the United States, he expects to see "the deterioration of this quintessentially strategic industry." ■

ELIOT MARSHALL

Science Policy Programs Progress

The study of the impact of science and technology on public policy took root in academe in the late 1950s and early 1960s. A new survey, "Graduate Education and Career Directions in Science, Engineering and Public Policy,"* reports that the field has prospered modestly but still faces some of its original problems.

The survey sponsored by the AAAS Committee on Science, Engineering, and Public Policy focuses on 21 programs† that provide professional training. It goes beyond previous inventories by reporting the results of a survey on how alumni of the programs have fared professionally.

Responses from about 550 of the 1500 alumni of the 21 programs show that, for many of them, their graduate training did lead to employment in their field and in jobs that many deem satisfactory. The principal employer from the start has been government, particularly the federal government.

A major hitch is that the alumni of the programs continue to have a professional identity problem. The report notes that there is "no single professional association or journal which might foster linkage among the graduates." And, so far, the field lacks a common curriculum. Therefore, as the report puts it, the enterprise lacks legitimacy in the academic world and prestige among employers.

As has been true from the start, the programs are divided sharply between those based in social science departments and those in engineering schools or departments. The latter require their students to have technical backgrounds—usually bachelor's degrees in science or engineering. The social science–based programs generally do not. Curriculum in the engineering-based programs typically stresses a quantitative approach (attempts at scientific methods of policy analysis), while the social science–based programs emphasize the qualitative, case study, approach. In both types of program, the master's is regarded as a professional degree and the Ph.D. as leading to academic employment or research.

While a few of the programs have gone

*Available from the AAAS Sales Office. $10.

†Institutions with programs in the survey are American University, Boston University, Carnegie-Mellon, Cornell, Dartmouth, Eastern Michigan, George Washington, Georgia Tech, Harvard, Indiana University, MIT, Rensselaer, Stanford, Syracuse, University of Denver, Michigan, Oklahoma, University of Texas at Austin, Vanderbilt, and Washington University.